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Remarks/Arguments:

With this amendment, the applicants amend claim 1 to correct a minor typographical error. No new matter has been added. Claims 1-7, 9, and 10 are pending.

The Office Action rejects claims 1-4, 9, and 10 under 35 U.S.C. § 102(b) as anticipated by Harris et al. (U.S. Patent 5,599,913). Claims 1, 4, and 5 stand rejected under 35 U.S.C. § 102(b) as anticipated by Suto (U.S. Patent 5,064,576). Claims 1-7, 9, and 10 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Wolfbeis et al. (U.S. Patent 5,407,829) in view of Moretti et al. as evidenced by Dojindo Online.

I. Present Invention

The present invention relates to sensing gaseous substances using metal complexes. Claim 1 recites "a metal co-ordinated complex immobilized in or on a substrate." Claim 1 also recites that the "complex, upon food spoilage or the opening or the compromise of packaging, undergoes a ligand exchange reaction to release a detectable component by the preferential binding of a gaseous substance to the metal of said complex." Claim 9 similarly recites the step of "inserting into or applying to said package or incorporating into a portion of the interior surface of said package, a metal co-ordinated complex immobilized in or on a substrate." Claim 9 also similarly recites that the "complex, upon food spoilage or the opening or the compromise of packaging, undergoes a ligand exchange reaction to release a detectable component by preferential binding of a gaseous substance to the metal of said complex."

This means that the metal complex undergoes a chemical reaction in which a ligand, such as fluorexon, complexed with a metal, such as palladium, undergoes a ligand exchange with another ligand such as sulfur compounds (e.g. sulphides) or nitrogen compounds (e.g. amines) present in spoiled foods in the gaseous phase, thus releasing a detectable component, such as a fluorexon. This released component is used to detect the food spoilage. This feature has advantages over current methods in that it enables the present invention to be suitable for use directly in the package, allowing continuous monitoring of food quality from packaging to consumption. The claimed invention overcomes the disadvantages of long evaluation times and sample destruction in currently used methods.

II. Lack of Anticipation

A. Harris et al. does not disclose metal-ligand complex chemistry

The Office Action rejects claims 1-4, 9, and 10 under 35 U.S.C. § 102(b) as anticipated by Harris et al. (U.S. Patent 5,599,913). The Office Action cites disclosures in Harris et al., but does not specifically point out how those citations teach each and every limitation of claim 1 of the present invention. The applicants need not address each citation in Harris et al. because the chemical reaction of the present invention is itself distinguishable from the reaction disclosed in Harris et al.

As discussed above, claim 1 recites a metal co-ordinated complex that undergoes a ligand exchange reaction to release the complex, which is a chromophore. The *Penguin Dictionary of Chemistry* defines a "ligand" as an entity from which electrons are donated, and a "complex" as any compound in which bonding is by interaction of the electrons of the donor (e.g. a ligand) with empty orbitals of the acceptor (e.g. a metal) (see attached).

Harris et al. does not disclose exhibiting a color change through release of the ligand in a metal-ligand complex. Harris et al. discloses a color change through release of a proton: "In the presence of alkali-metal ions and a base, a proton comes off the nitrophenol hydroxy group [of the chromoionophore, see e.g. formulas V, VI and VII] causing a colour change" (see column 6, lines 46-48). The Harris et al. reaction involves an exchange of ions, i.e. a proton exchange for a lithium salt of the chromoionophore defined by formulas V, VI and VII. Such a reaction is not that of a complex/ligand exchange reaction as recited by claim 1 of the present invention. Method claim 9 recites substantially the same limitations of claim 1 as discussed above. Therefore, because Harris et al. neither discloses nor suggests the limitations of the present invention as claimed by claims 1 and 9, the applicants submit that none of the claims are anticipated by Harris et al.

B. Soto does not teach detecting food spoilage products

The Office Action rejects claims 1, 4, and 5 under 35 U.S.C. § 102(b) as anticipated by Suto (U.S. Patent 5,064,576). Suto is directed to a steam sensitive composition and a sterilization indicator composition. Suto discloses a color indicator for detecting when sterilization is complete, that is, when no food spoilage gases are present. In contrast, claim 1 recites "a sensor for detecting food spoilage products within food packaging or the opening or

compromise of packaging," i.e. a sensor suitable for such a purpose as claimed in the present invention. Additionally, the chemical reaction taught by Suto is different from the present invention. Suto discloses a "ligand-displacement reaction which proceeds only under steam sterilization steam conditions" (see column 2, lines 30-32, emphasis added). Steam sterilization conditions include exposure to "time, temperature and steam." Col. 2 lines 65 and 66. It is implicit that the detection of food spoilage or the opening or compromise of packaging according to claim 1 occurs at ambient temperatures or below, e.g. where the food is chilled. Therefore, the ligand-displacement reaction taught by Suto is completely unsuitable for use in the present invention. Thus, Suto does not anticipate independent claims 1 and 9.

III. Non obviousness

The Office Action rejects claims 1-7, 9, and 10 under 35 U.S.C. § 103(a) as being unpatentable over Wolfbeis et al. (U.S. Patent 5,407,829) in view of Moretti et al as evidenced by Dojindo Online. In view of the arguments below, the applicants respectfully disagree.

In forming the obviousness rejection, the Office Action suggests that the motivation to combine Wolfbeis et al. with Moretti et al. is that "one would have been substituting one conventional fluorescence sensor for another of the same purpose: detection of sulfur compounds by measuring a change in fluorescence" (see paragraph 11 of the Office Action). "There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998) (The combination of the references taught every element of the claimed invention, however without a motivation to combine, a rejection based on a *prima facie* case of obvious was held improper.).

The problem solved in the present invention is different from Moretti et al., which is also different from Wolfbeis et al. The present invention solves the problem of detecting food spoilage through a colorimetric indicator. Moretti et al. solves the problem of detecting cattle illegally treated with thyrostatic drugs (page 459). Wolfbeis et al. solves the problem of visual detection of sterilized containers. Thus, no motivation to combine these references can be gleaned from the nature of the problem to be solved because the problems solved are all different.

There is no disclosure in Moretti et al. or Wolfbeis et al. to combine the detection of cattle illegally treated with thyrostatic drugs of Moretti et al. with a colorimetric system to detect when items are sterilized as in Wolfbeis et al. Thus, there is no motivation to combine the references from the teachings of the prior art.

The knowledge of persons of ordinary skill in the art also do not provide the motivation to combine the cited prior art references because of the vast differences between the references as describe above.

Therefore, the Office Action fails to establish a *prima facie* case of obviousness because the rejection lacks a proper motivation to combine the references. That is, there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the reference teachings. In particular, there is no teaching or suggestion in the prior art to make the claimed combination, except with the knowledge and hindsight gleaned from applicants' own disclosure.

At paragraph 8 of the Office Action, the Office Action states, "Although Wolfbeis et al. teach the sensors change their fluorescence in response to sulfur containing gases, Wolfbeis et al. [is] silent in teaching they undergo a ligand exchange *per se*." Since Wolfbeis et al. is silent in teaching that the sensors undergo a ligand exchange *per se*, it is hindsight to adopt this feature from the applicants' disclosure and then to look for documents that teach sensors that undergo a ligand exchange *per se* in an effort to show that the claimed invention is obvious.

Further, it is hindsight to suggest that a skilled person would combine a document that teaches a sensor for detecting gas phase spoilage products (Wolfbeis et al.) with a document teaching "wet" analysis of bovine thyroid gland samples (Moretti et al., see under "Extraction and clean up," Preparation of spray reagent" headings and under the "Chromatography" second paragraph). The applied references have been improperly combined, using hindsight reconstruction, without evidence to support the combination.

IV. Conclusion

The present invention is not anticipated by Harris et al or Suto. The chemical reaction in Harris et al. is not a metal-ligand complex reaction. Suto discloses a detection sensor to determine when items are made sterile by exposure to temperature and steam. Neither Harris et al. nor Suto disclose or suggest the present invention. The present invention is not obvious

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Reply to Office Action of November 10, 2003

JMYT-233US

in view of Wolfbeis et al., Moretti, and Dijindo. The Office Action failed to present a proper *prima facie* case for obviousness and has improperly used hindsight gleaned from applicants' application. In view of the arguments set forth above, the applicants respectfully request withdrawal of the rejections and request early notification of allowance.

Respectfully submitted,



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CMB/lrb

Enclosures: Pgs. 106 and 238 of the
"Penguin Dictionary of Chemistry,"
Second Edition (1990)

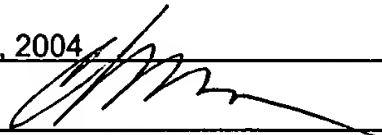
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**An abridged edition of *Miall's Dictionary of Chemistry 5th Edition*,
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colour photography The process of preparation of prints or transparencies in colour. White light is split into three components – red, green and blue – by filters – yellow, magenta, cyan. The particular colour activates grains of silver halide (generally in specific layers for each colour) which contain sensitizing dyes on the grain. Colour development* then gives rise to a coloured image.

columbite (Fe, Mn)(Nb, Ta)₂O₆ with excess Nb. The principal ore of niobium*.

columbium, Cb. A former name and symbol for niobium*.

combining volumes, law of See Gay-Lussac's law.

combustion The rapid, high-temperature oxidation of fuels, converting carbon to carbon dioxide (or carbon monoxide) and hydrogen to water vapour. Any sulphur in the fuel is oxidized to the dioxide or trioxide depending on combustion conditions, while nitrogen either remains unreacted or is converted to nitrogen oxides. Most combustion reactions occur in the gas phase except for the burning of the fixed carbon in solid fuels.

The release of chemical energy during combustion of gases produces a luminous, radiating zone which is seen as the flame or flame front*.

common-ion effect In a solution of a weak electrolyte, e.g. ethanoic acid, the concentration of ions is governed by the equilibrium



Addition of excess H⁺ ions to this solution will cause the equilibrium to move towards undissociated acid thereby decreasing the concentration of A⁻. This effect is known as the common-ion effect and is of considerable practical importance. Thus, e.g. in the precipitation of metal ions as insoluble sulphides, the concentration of S²⁻ in aqueous solution is controlled by the equilibrium



Addition of acid will reduce the concentration of S²⁻, whilst in alkaline solution the concentration of S²⁻ will increase. Since, in order for precipitation to occur, the solubility product of the sulphide must be exceeded, i.e.

$$K_{sp} = [\text{M}^{x+}][\text{S}^{2-}]^{x/2}$$

the actual precipitation can be controlled by varying the pH of the solution.

complement The combination of an antibody and an antigen* on the surface of a foreign

cell leads to the 'fixation' of a group of proteins present in normal serum, collectively known as complement. The result is the activation of destructive enzymes which cause lysis of the cell.

complex Any compound in which the bonding is by interaction of the electrons of the donor with empty orbitals of the acceptor. In some complexes the electron flow may take place in both directions simultaneously – see back-bonding. The interaction may take place between charged or uncharged species.

Where the structure is known a complex species comprising the acceptor and its ligands is formulated within square brackets, e.g. [Co(NH₃)₆]Cl₃. Bridging ligands are designated μ -L, e.g. Fe₂(CO)₉ is [(OC)₃Fe(μ -CO)₃Fe(CO)₃]. Hapto designates the number of ligand atoms actually bonded to the acceptor, e.g. [(h⁵-C₅H₅)Mn(CO)₃] has 5 carbon atoms (plus 3 carbonyls) bonded to manganese.

complex ion A complex ion is formed by the co-ordination of other ions or molecules to an ion or atom to form a stable charged entity. Thus the Co³⁺ ion and ammonia give [Co(NH₃)₆]³⁺ whilst the Fe³⁺ ion and cyanide ions give the [Fe(CN)₆]³⁻ complex. Depending upon the stability of the complex a solution of a complex salt may or may not give the reactions of the individual components of the complex. It should be noted that hydrated salts generally contain aquo-complexes, e.g. [Cu(H₂O)₆]²⁺ and that the anions of oxy-salts may be considered as being complexes formed by (mostly hypothetical) positive ions and oxide ions, e.g. the NO₃⁻ ion as N⁵⁺ and 3O²⁻.

complexometric indicator See metallochromic indicator.

complexometric titration A titration* involving formation or decomposition of a complex. Thus Fe³⁺ plus SCN⁻ is intense red; titration of the Fe³⁺ with EDTA causes decomposition of the red Fe³⁺-SCN⁻ complex and formation of the colourless Fe³⁺-EDTA complex.

complexone See sequestering agent.

component For the phase rule* the number of components in a chemical system is the smallest number of substances in terms of which the compositions of each of the phases in the system may be described separately. The number of components in a system need not necessarily equal the number of chemical species present. For example, if calcium carbonate is heated in a closed system:



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Lewis acid See acid.

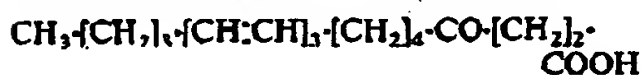
Lewis base See base.

lewisite, 2-chlorovinylchloroarsine, 1-chloro-2-dichloroarsino-ethene, $C_2H_2AsCl_3$, $ClCH:CH-AsCl_2$. A pale yellow liquid, m.p. $-13^\circ C$, b.p. $190^\circ C$. It has a strong smell, resembling that of geraniums. War gas, systemic poison. It is hydrolysed by water and also destroyed by alkalis and by oxidizing agents. It can be manufactured by bubbling ethyne through a mixture of anhydrous arsenic trichloride and aluminium chloride.

Li Lithium.

libration In a crystalline lattice the rotational motions of molecules within the lattice may be restricted due to bonding with neighbouring atoms. The resulting rotational oscillations of the whole molecule are called librational modes.

licanic acid, $C_{18}H_{28}O_3$. White crystals.



The naturally occurring isomer, α -licanic acid, has m.p. $74-75^\circ C$. It is unstable, and is readily isomerized to the β -form, m.p. $99.5^\circ C$. It occurs in oiticica and other oils which were previously used in the protective-coating industry.

Liebermann's reaction A colour-test for $-NO$ or $-OH$ groups. For the detection of an $-NO$ group a small quantity of the substance is dissolved in concentrated sulphuric acid and a crystal of phenol added. A blue-green colour develops on warming, this changes to red on pouring into water, and back to blue with excess of alkali. When the test is used for detecting a phenol, the substance and a crystal of sodium nitrite are dissolved in sulphuric acid and warmed. On dilution and addition of alkali many phenols give distinctive colours.

lift-off In gas burners having a stationary flame it is essential that the flame speed of the combustible mixture should be balanced by the velocity of the mixture in the burner tube or flame ports. If the flame speed is too low or the mixture velocity too high the flame can lift-off the burner mouth or flame ports.

ligand A complexing group in co-ordination chemistry. Generally the entity from which electrons are donated. NH_3 is a ligand in $[Co(NH_3)_6]Cl_3$.

ligand field theory An extension of crystal-field theory which takes account of electron transfer.

light-heavy selectivity In solvent extraction the phenomenon in which the extractive power of the solvent is dependent on the molecular weight of the component extracted.

light scattering The scattering of light by suspended particles. Can be used to estimate molecular weights of macromolecules and to detect end-points when a precipitate is formed in the reaction.

light stabilizers See ultra-violet absorbers.

lignans A group of natural products obtained by ethereal or alcoholic extraction from the wood or exuded resin of the *Coniferae* and other plants, and characterized by the presence in the molecule of the 2,3-dibenzylbutane skeleton.

lignin A highly polymeric substance occurring with cellulose in lignified plant tissues. It is largely responsible for the strength of wood, which contains 25-30 %, and it is extractable from wood pulp by the action of SO_2 and lime-water: it occurs (up to 6 %) in sulphite waste liquors from paper mills. Lignin is a phenyl propene polymer of variable mol.wt. It is of commercial value as a source of vanillin, phenols and other aromatic chemicals. Used as a filler for plastics and as a dispersant, emulsifier, etc.

lignite, brown coal Immature coals intermediate in composition between peat and bituminous coals. They occur in thick seams, often quite near the earth's surface.

lignoceric acid, $C_{24}H_{48}O_2$. M.p. $84^\circ C$. Fatty acid present free and combined in many oils, fats and waxes but principally tall oil.

lignrin Essentially petroleum ether: strictly that fraction of refined naphtha with b.p. $80-130^\circ C$. Contains aliphatic hydrocarbons and is used as a solvent.

lime See calcium hydroxide and calcium oxide.

limestone Rocks of sedimentary origin containing the remains of marine organisms or chemically precipitated or transported calcium carbonate. The pure mineral consists of $CaCO_3$ in the form of calcite, but is rarely found. Commercial limestone contains iron oxide, alumina, magnesia, silica and sulphur, with a CaO content of 22-56 % and a MgO content of up to 21 %. It is used as such as a fertilizer and for many other purposes, or is calcined to calcium oxide.

limewater See calcium hydroxide. Used as a

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